Preparation of Methyl Acetoxypropionate

REACTION OF LACTIC ACID WITH METHYL ACETATE

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Lactic acid can be made in almost unlimited quantities by fermentation of abundant, low-cost carbohydrates. A one-step method is described for transforming lactic acid into methyl acetoxypropionate. The reaction between lactic acid of various concentrations and methyl acetate is studied under different conditions to determine the effect of variables on the yield of methyl acetoxypropionate. Both methyl lactate and methyl acetoxypropionate are produced. Under some conditions 63.6 and 28.4% yields, respectively, of methyl lactate and methyl acetoxypropionate were obtained. This preparation of methyl acetoxypropionate requires less acetic anhydride or ketene than the customary method, which consists in treating methyl lactate with either acetic anhydride or ketene. Physical and chemical properties of methyl lactate and its azeotrope with water are described.

EFFICIENT and inexpensive methods of converting lactic acid (*27*, *28*, *29*) into its diester, methyl α-acetoxypropionate (I), are highly desirable since on pyrolysis methyl α-acetoxypropionate yields methyl acrylate and acetic acid (*5*, *12*, *21*, *22*, *29*). The preparation of methyl acrylate, an important synthetic rubber (*1*, *6*, *9*, *10*, *23*, *24*, *30*, *35*) and resin (*16*) intermediate, by pyrolysis of the acetyl derivative (I) of methyl lactate, is attractive because lactic acid can be made at low cost by fermentation of several abundant carbohydrates:

$$HOCH(CH_3)COOH + CH_3COOCH_3 \longrightarrow CH_3COOCH(CH_3)COOCH_3 + H_2O$$
(I)

$$CH_3COOCH(CH_3)COOCH_3 \xrightarrow{\text{pyrolysis}} CH_3COOH + CH_2{:}CHCOOCH_3$$
(I)

Methyl acetoxypropionate is usually made by the two separate operations of esterifying lactic acid (*11*, *13*, *26*, *28*, *34*) with methanol and acetylating the resulting methyl lactate with acetic anhydride (*5*, *29*), ketene (*7*), or acetyl chloride (*18*). The reaction of lactic acid with methyl acetate was studied in the present work because it seemed probable that lactic acid would be converted into methyl acetoxypropionate in one operation. At the beginning of the study it appeared that the direct transformation of lactic acid into methyl acetoxypropionate in this manner would have the following advantages: (*a*) One step of previous syntheses would be eliminated and thereby reduce the cost of manufacture; (*b*) less equipment would be required; (*c*) corrosion of equipment would be less troublesome; and (*d*) the use of acetic anhydride, ketene, or acetyl chloride would not be required.

The reaction of lactic acid with methyl acetate is of interest also because it involves an unusual type of ester interchange; i.e., one of the reactants is bifunctional and can enter into both alcoholysis and acidolysis reactions. The reaction between lactic acid and methyl acetate is more complex than would be realized on first consideration because the usual grades and concentrations of lactic acid consist of a mixture (*2*, *3*, *33*) of monomeric lactic acid, water, and condensation products of lactic acid, such as lactyllactic acid, $HOCH(CH_3)COOCH(CH_3)COOH$. Isolation of the products was found to be rather difficult because of the presence of several components, one of which (methyl lactate) hydrolyzes easily and distills azeotropically with water.

Powers (*19*) reported that ethyl acetoxypropionate was obtained by treating lactic acid with ethyl acetate, but he did not give yields or the concurrent formation of ethyl lactate.

PROPERTIES OF METHYL LACTATE

In the earlier stages of the investigation the yields of methyl lactate varied widely, and the experiments could be reproduced only with difficulty. To determine whether these erratic results were due to condensation or hydrolysis reactions during distillation, a study of the stability of methyl lactate under various conditions was made. Possible side reactions considered were hydrolysis to lactic acid and methanol, conversion into its condensation polymers (II), and decomposition into acetaldehyde, carbon monoxide, and methanol:

$$nHOCH(CH_3)COOCH_3 \longrightarrow H[OCH(CH_3)CO]_nOCH_3 + (n-1)CH_3OH$$
(II)

CONDENSATION REACTIONS. Methyl lactate was refluxed for 3 hours with anhydrous zinc sulfate, calcium sulfate, sodium sulfate, sodium acetate, sulfuric acid, and lactic acid (100% concentration). Methyl lactate was not appreciably affected by this treatment in the presence of the salts or lactic acid, but sulfuric acid was highly active in promoting condensation. On distillation of the reaction mixture obtained from one drop of sulfuric acid and 75 ml. of methyl lactate, there were obtained methanol 46 ml. of methyl lactate and 20 ml. of viscous distillation residue (probably methyl esters of linear condensation products of lactic acid). Presumably other strong acids would have a similar effect.

HYDROLYSIS. Considerable hydrolysis occurs when methyl lactate containing water is distilled at atmospheric pressure, even in the absence of catalysts. The lactic acid produced by the hydrolysis was recovered as distillation residue, which probably consisted of lactic acid condensation polymers (*2*, *3*, *33*). Mineral acids catalyzed the hydrolysis most effectively. The effect of buffers was not studied thoroughly, but the addition of an alkaline agent, such as sodium acetate, retarded hydrolysis even in the apparent absence of mineral acid. As was to be expected, hydrolysis was negligible when the distillation was carried out under reduced pressure (approximately 50 mm.) in the absence of catalysts.

WATER–METHYL LACTATE AZEOTROPE. Prior to publication of Weisberg and Stimpson's patent (*34*), it was observed that water and methyl lactate distill as a constant-boiling mixture whose composition varies with the distillation pressure. Determination of the composition of the azeotrope was complicated

TABLE I. DENSITIES OF METHYL LACTATE

Source	0° C.	10.7° C.	13° C.	15° C.	19° C.	20° C.	26° C.	30° C.
Equation 1	1.1162	1.1046	1.1013	1.0989	1.0943	1.0932	1.0862	1.0818
(25)	1.1180	..	..	..	1.0898	..	..	..
(36)	..	1.1037	..	..	..	..	1.0857	..
(31)	..	..	1.100	..	..	..	..	..
(8)	..	..	..	1.097	..	1.093	..	..
(32)	..	..	..	..	..	1.0895	..	1.0785
(20)	..	..	..	..	..	1.0925	..	..
Present work	..	..	..	..	..	1.0928	..	1.0825

by hydrolysis of methyl lactate, but it was found that under atmospheric pressure the azeotrope contains 25 to 30% methyl lactate and distills at 99° to 99.5° C. When distilled at 38–39° under a pressure of 50–52 mm., the azeotrope contained 12 to 15% of methyl lactate.

Benzene and methyl lactate did not distill azeotropically, and benzene, water, and methyl lactate did not form a constant-boiling ternary mixture. Hence benzene is suitable for removing water from methyl lactate by distilling the benzene-water binary azeotrope. Methyl lactate can also be recovered from aqueous solution by extraction with benzene, ether, or other suitable solvent.

PHYSICAL CONSTANTS. The density data of Patterson and coworkers (*17*, *18*), which were determined at temperatures from −74° to 125° C., are defined satisfactorily by Equation 1:

$$\text{density} = (967.34 - t^\circ \text{ C.})/866.67 \qquad (1)$$

Other density data are recorded in Table I.

Refractive index data (n_D^t) determined in this laboratory with the redistilled methyl lactate referred to in Table I are: 1.4183 (10° C.), 1.4162 (15°), 1.4141 (20°), 1.41263 (23.5°), and 1.4120 (25°). The following refractive indices have been reported: 1.413 at 20°, Godchot and Vieles (*14*); 1.4149 at 19°, Burkard and Kahovec (*4*); 1.4132 at 25°, Smith and Claborn (*26*).

The molecular refraction of our sample, calculated from the refractive index of 1.4141 and density of 1.0928, was 23.82 instead of the theoretical value of 23.85. The relation between temperature and the refractive indices determined in the present work is given by Equation 2:

$$n_D^t = 1.4225 - 0.00042\,t \qquad (2)$$

Several boiling points of methyl lactate, observed in this laboratory, are plotted against pressure in Figure 1.

EXPERIMENTAL PROCEDURE

Commercial lactic acid samples of 80 and 100% concentration, which were edible and almost colorless, were used. The concentrations were verified by neutralization and saponification of a known quantity of sample with standard solutions of sodium hydroxide.

Concentrations of lactic acid above 100% were obtained by the dehydration of 80 or 100% acid. This can be effected by refluxing the acid with an entraining agent (*33*) such as benzene, which removes water azeotropically, or by heating the acid in a vacuum to distill both the "free water" and that formed by self-esterification (*2*, *3*, *11*). The acid used in experiments 21, 36, and 37 was dehydrated with benzene and without catalyst. It was a clear, transparent, brown, very viscous, resinlike material, the concentration of which was calculated from its saponification equivalent. That used in experiments 23, 24, and 25 was prepared with benzene and with sulfuric acid as a catalyst; its concentration was calculated from the amount of water removed from the 100% acid used as starting material.

High-pressure bombs designed for hydrogenation work were used for the ester-interchange experiments. They were electrically heated, and the temperatures were controlled and recorded automatically. In experiments 17, 18, and 22, a 183-cc. unlined stainless steel bomb was used; in experiments 8, 27, 28, 36, and 37, a 2240-cc. bomb with Pyrex liner was used; in all other experiments a 1270-cc. bomb with brass liner was used. The two larger bombs were made of high-carbon manganese steel. The two smaller bombs were rocked continuously during the heating periods; no agitation was used with the larger one. Agitation produced no detectable effect on the yields. Mild corrosion of the bombs was observed at 180° C., which became more pronounced at higher temperatures or when acetic acid was included in the charge. The pressures developed in the 180° and 220° C. experiments were 250 to 275 and 475 to 500 pounds per square inch, respectively.

The reaction mixtures were carefully distilled through efficient columns, usually a twenty-plate Lecky-Ewell still (*15*). A Vigreux column, 15 mm. in diameter and 800 mm. long, gave results agreeing closely with those from the more efficient still, although the purity of the various fractions was much lower. Very careful and efficient fractionation is required for good separation of the components: (1) methyl lactate–water azeotrope, boiling point 99.5° C.; (2) acetic acid, 118°; (3) methyl lactate, 144–5°; and (4) methyl α-acetoxypropionate, 171–2°. In some experiments the entire distillation was conducted at atmospheric pressure; in others the pressure was reduced to about 50 mm. when fraction 1 was reached. Operation at reduced pressure has the advantages that less methyl lactate is removed in fraction 1 and also less lactate is lost by hydrolysis and condensation. In either case it is essential to neutralize the acid catalyst before distillation, a slight excess of sodium acetate being used for this purpose in the present work.

INTERACTION OF LACTIC ACID AND METHYL ACETATE

Although a considerable quantity of methyl acetoxypropionate was formed by the reaction of lactic acid with methyl acetate, the principal product was methyl lactate. The reproducibility of the results, which was not entirely satisfactory, is indicated by experiments 1 to 8, Table II. Possibly the lack of reproducibility can be attributed to the use of relatively small quantities of reagents and the catalytic effect of the bomb or liner walls on the reaction. Experiments in which larger amounts of reagents were used are more significant, partly because smaller quantities were used early in the investigation when some of the difficulties encountered were not fully appreciated.

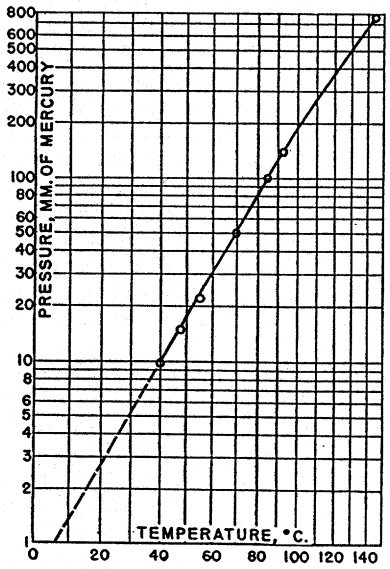

Figure 1. Vapor Pressure of Methyl Lactate

The total yields of esters obtained with methyl acetate (Table II) were as high as the yields of methyl lactate observed in the direct esterification of lactic acid with methanol. Considerable quantities of methyl acetoxypropionate and moderately high yields of methyl lactate were obtained when 1 mole of lactic acid was heated with 12 moles of methyl acetate at 180° C. for 4 hours (in the presence of a small amount of catalyst). The yields of methyl lactate and methyl acetoxypropionate observed under these conditions (63.6 and 28.4%, respectively) were obtained in experiment 27, in which larger amounts of the reactants were

TABLE II. REACTION OF LACTIC ACID WITH METHYL ACETATE

Expt. No.	Lactic Acid Concn., %	Lactic Acid Moles	Ratio, Ester: Acid	Catalyst	Additional Reactants, Moles	Time, Hr.	Temp., °C.	Conversion, % Into methyl lactate	Conversion, % Into methyl acetoxypropionate	Conversion, % Combined esters
1	100	0.67	6	H_2SO_4, 5 drops	None	4	180	43.2	17.9	61.1
2	100	0.67	6	Same	None	4	180	38.4	10.1	48.5
3	100	0.67	6	Same	None	4	180	53.6	12.4	66.0
4	100	0.67	6	Same	None	4	180	50.2	11.7	61.9
5	100	0.67	6	Same	None	4	180	51.5	14.0	65.5
6	100	0.67	6	Same	None	4	180	50.3	22.4	72.7
7	100	0.67	6	Same	None	4	180	60	17.3	77.3
8	100	2.0	6	H_2SO_4, 10 drops	None	4	180	55.0	24.7	79.7
9	100	0.67	6	Toluenesulfonic acid, 1 g.	None	4	180	43.4	11.1	54.5
10	100	0.67	6	Toluenesulfonic acid, 1 g.; H_2SO_4, 2 drops	None	4	180	46.5	23.0	69.5
11	100	0.67	6	H_2SO_4, 5 drops	None	2	180	41.5	3.4	44.9
12	100	0.67	6	Same	None	5.5	180	64.5	14.5	79.0
13	100	0.67	6	Same	None	8	180	64.5	17.3	81.8
14	100	0.67	6	Same	None	45	180	48.8	28.5	77.3
15	100	0.67	6	Same	None	4	150	50.2	0.0	50.2
16	100	0.67	6	Same	None	4	212	43.2	22.4	65.6
17	100	0.245	5.3	H_3PO_4, 1 ml.	None	3.5	260	49.0	13.3	62.3
18	100	0.5	2	Toluenesulfonic acid, 1 g.	None	4	180	34.4	11.5	45.9
19	100	1.00	2	H_2SO_4, 5 drops	None	4	220	27.2	12.7	39.9
20	100	1.00	3	Same	None	4	220	54.3	15.7	70.0
21	118	1.00	3	Same	None	7	140	29.8	5.2	35.0
22	100	0.3	4	Toluenesulfonic acid, 1 g.	None	4	180	22.7	15.8	38.5
23	120	1.0	4	Same	None	4	180	16.8	7.4	24.2
24	120	1.0	4	Same	None	4	180	10.4	0	10.4
25	120	1.0	4	H_2SO_4, 5 drops	None	4	180	1.8	0	1.8
26	80	0.75	4	Same	None	4	180	47.4	7.0	54.4
27	100	1.0	12	H_2SO_4, 10 drops	None	4	180	63.6	28.4	92.0
28	80	2.0	6	Same	None	4	180	64.4	11.2	75.6
29	118	1.0	2	H_2SO_4, 5 drops	Acetic acid, 1	7	140	6.1	3.2	9.3
30	100	1.0	3	Same	Same	7.5	210	36.7	15.7	52.4
31[a]	100	0.67	6	Same	Same	8	210	39.2	21.3	60.5
32[a]	100	0.67	6	Same	Same	8	210	36	..	..
33	100	0.67	6	Same	Acetic anhydride, 0.33	4	180	31.3	16.3	47.6
34	100	0.67	6	Same	Methyl lactate, 0.5	4	180	14.2	16.8	31.0
35	100	2.00	6	H_2SO_4, 10 drops	Methanol, 4	4	180	75.5	7.9	83.4
36	117	2.0	0	Same	Methanol, 12; acetic acid, 12	4	180	46.7	3.7	50.4
37	117	2.0	5	Same	Methanol, 2; acetic acid, 2	4	180	44.7	10.0	54.7

[a] A bulky white solid, possibly lactide, was obtained.

used. Examination of the results obtained in experiments 18, 22, 8, and 27 indicates that the formation of esters at 180° is favored by the use of increased proportions of methyl acetate.

Operating under the conditions of experiment 27 would give a total conversion of 92.0%, of which 38% by weight is methyl acetoxypropionate. Although the use of methyl acetate, as exemplified by experiment 27, would not eliminate entirely the use of acetic anhydride or ketene, the quantity of these acetylating agents required would be less. Probably a large proportion of the distillation residues obtained in experiments 1 to 8 could be converted into methyl lactate by treatment with methanol or into lactic acid by hydrolysis.

The results of experiments 8, 9, 10, 17, 18, 19, 22, 24, 25, and 26 may be used to compare sulfuric acid, phosphoric acid, and *p*-toluenesulfonic acid as catalysts, but definite conclusions do not appear warranted. Since *p*-toluenesulfonic acid is used in larger quantities, however, it can be concluded tentatively that sulfuric acid is preferable on a weight and cost basis.

It appears from experiments 8, 11, 12, 13, and 14 that the yields of esters increase with time of reaction (at 180° C.) up to approximately 4 hours, and that the use of longer periods has little effect on the total yield of esters.

Comparison of experiments 15 and 16 suggests that methyl lactate is formed at relatively low temperatures but that the formation of methyl acetoxypropionate is favored by more drastic conditions.

Experiments 22 to 25 show that 100% lactic acid gives higher yields of esters than polylactic acid under the same conditions. It appears from experiments 25, 26, and 28 that 80% lactic acid also is preferable to polylactic acid.

Judging from experiments 29 to 37, the value of using certain third components seems questionable. Acetic acid and acetic anhydride were used to determine whether increased yields of methyl acetoxypropionate would result. The purpose of using methyl lactate (experiment 34) was to ascertain the feasibility of recycling the methyl lactate in order to obtain a higher ultimate yield of methyl acetoxypropionate. The effect of using methanol (experiment 35) was to lower the yield of methyl acetoxypropionate.

It might be expected that polylactic acid, methanol, and acetic acid would react to give results comparable to those obtained by treating lactic acid with methyl acetate. Experiments 36 and 37 show that acetic acid and methanol cannot be substituted satisfactorily in this manner for methyl acetate when the mixture is heated at 180° C. for 4 hours. Possibly the same equilibrium mixture would result under more drastic conditions.

Several conclusions on the mechanism of the reactions involved seem warranted. When monomeric lactic acid and methyl acetate are the reactants, the following reactions, along with others, are to be anticipated:

$$HOCH(CH_3)COOH + CH_3COOCH_3 \rightleftharpoons HOCH(CH_3)COOCH_3 + CH_3COOH \quad (3)$$

$$HOCH(CH_3)COOH + CH_3COOCH_3 \rightleftharpoons CH_3COOCH(CH_3)COOH + CH_3OH \quad (4)$$

$$HOCH(CH_3)COOCH_3 + CH_3COOCH \rightleftharpoons CH_3COOCH(CH_3)COOCH_3 + CH_3OH \quad (5)$$

$$HOCH(CH_3)COOCH_3 + CH_3COOH \rightleftharpoons CH_3COOCH(CH_3)COOCH_3 + H_2O \quad (6)$$

$$CH_3COOCH(CH_3)COOH + CH_3COOCH_3 \rightleftharpoons CH_3COOCH(CH_3)COOCH_3 + CH_3COOH \quad (7)$$

$$CH_3COOCH(CH_3)COOH + CH_3OH \rightleftharpoons CH_3COOCH(CH_3)COOCH_3 + H_2O \quad (8)$$

Inasmuch as lactic acid, a secondary alcohol, would be expected to react sluggishly in alcoholysis reactions (Equation 4) and methyl lactate was the principal product, probably reaction 3 predominated over reaction 4. Acetoxypropionic acid was present in negligible or small quantities, and therefore it seems likely that it was not formed in significant amounts or that it was transformed readily (via reaction 7 or 8) into methyl acetoxy-

propionate. Since all the methyl acetate reactions (Equations 3, 4, 5, and 7) are beneficial, the importance of using large proportions of this ester is clear. Inasmuch as the use of acetic acid with methyl acetate was not helpful (experiments 29 to 32), probably reaction 6 plays a minor role. Acetic acid would be actually detrimental if its presence caused reactions 3 and 7 to be reversed.

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